

Role of epidural neostigmine in prevention & management of post-dural puncture headache in women after delivery by Caesarean section using spinal anesthesia

A Thesis study

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CONTENTS

<i>Contents</i>	<i>I</i>
<i>Abstract & Keywords</i>	<i>II</i>
<i>Aim of work</i>	<i>IV</i>
<i>List of tables</i>	<i>V</i>
<i>List of figures</i>	<i>VI</i>
<i>List of abbreviations</i>	<i>VII</i>
<i>Review of literature</i>	
<i>Introduction</i>	<i>1</i>
<i>Related anatomy</i>	<i>4</i>
<i>Pathogenesis of PDPH</i>	<i>14</i>
<i>Management of PDPH</i>	<i>26</i>
<i>Nature of neostigmine and anticholine estrases</i>	<i>43</i>
<i>Neostigmine analgesia</i>	<i>49</i>
<i>Materials and Methods</i>	<i>66</i>
<i>Results</i>	<i>73</i>
<i>Discussion</i>	<i>81</i>
<i>English summary</i>	<i>88</i>
<i>References</i>	<i>90</i>

Abstract

Controlling the occurrence of undesirable side effects following spinal anesthesia is very important especially for women undergoing delivery by caesarian section (CS). Post dural puncture headache (PDPH), being one of the most distressing side effects interfering with the life style of the new mother as well as her ability to take care of her baby. Post dural puncture headache (PDPH) is linked to spinal anesthesia as a side effect since Karl August Bier, German surgeon, performed the first spinal anesthesia in 1898. Bier injected cocaine into the subarachnoid space of seven patients, himself and his assistant. Bier, his assistant and four of the subjects all described the symptoms associated with PDPH. Many factors may affect the occurrence of Post dural puncture headache PDPH, with many management options.^(1, 2)

Neostigmine, a well-known drug that is used frequently in the anesthetic practice, is found to have analgesic properties especially when used via the central routes as intra thecal (IT) and epidural routes, causing a state of analgesia and sedation. This analgesic effect is attributed to the anti-nociceptive effect of the drug. Therefore, epidural neostigmine may interfere with the pathogenesis of post dural puncture headache (PDPH).

In this study, we tried to uncover the role of epidural neostigmine in preventing and controlling symptoms of post dural puncture headache (PDPH) in women underwent delivery by caesarian section (CS) using spinal anesthesia, also the analgesic and sedative effects of the drug were observed. Comparing two doses of the drug and assessing their effect and potential side effects in order to reach an optimum dose producing accepted reasonable effects with the least accepted side effects.

Keywords:

- Spinal anesthesia
- PDPH
- Cesarean Section
- Epidural Neostigmine

Aim of work

To prove or disprove the value of epidurally administered neostigmine in preventing and managing PDPH, allowing its subsequent use as an active agent in preventing and controlling this condition. As well as monitoring of other desirable effects and also possible side effects and whether their occurrence is related to the dose of neostigmine, trying to reach optimum dose obtaining the desired effects with minimal side effects.

LIST OF TABLES

	<u>Page</u>
Table 1. Bromage scale	69
Table 2. Demographic data: Comparison between the three groups	75
Table 3. Comparison between the onset and duration of headache in the three groups.	75
Table 4. The maximum severity of headache between the three studied groups in different positions	76
Table 5. The time of first analgesic request & total dose of paracetamol	76

LIST OF FIGURES

	Page
Figure 1.The vertebral column	4
Figure 2. The intrecrestal (Tuffier’s) line crossing through L4 spine	5
Figure 3 Anatomy of the vertebra	5
Figure 4.The intervertebral disc	6
Figure 5.The ligaments and intervertebral discs joining adjacent vertebrae	7
Figure 6.The spinal meninges	8
Figure 7. Cross sectional lumbar details	11
Figure 8. Graphical representations of epidural (needle 4) and spinal needle tip design	18
Figure 9. Scheme for synthesis of neostigmine	44
Figure 10. Ball and stick model of neostigmine molecule	45
Figure 11.Muscarinic receptors	51
Figure 12. Injection in the epidural space	68
Figure 13.Identification of lumbar interspaces using Tuffier’line	68
Figure 14.Loss of resistance technique	68
Figure 15. The incidence of PDPH in the three groups	77
Figure 16.The incidence of sedation in the three studied groups	77
Figure 17.Heart rate changes in the three groups over the first 24 hours	78
Figure 18. Mean arterial blood pressure changes in the three groups over 24 hours	78
Figure 19.The incidence of nausea in the three studied groups	79
Figure 20.The incidence of vomiting in the three studied groups	79

LIST OF ABBREVIATIONS

<u>%</u>	Percent
<u>&</u>	And
<u>±</u>	Minus or plus
<u>®</u>	Registered trade mark
<u>°C</u>	Degree Celsius
<u>µg</u>	Microgram
<u>5-HT1D</u>	5- hydroxyl tryptamine 1 D
<u>Ach</u>	Acetylcholine
<u>AChRs</u>	Acetyl choline receptors
<u>ACTH</u>	Adrenocortical trophic hormone
<u>AED</u>	Antiepileptic drug
<u>ASA</u>	American society of anesthesiology
<u>C</u>	Cervical
<u>cm</u>	Centimeter
<u>CNS</u>	Central nervous system
<u>CS</u>	caesarian section
<u>CSF</u>	Cerebro spinal fluid
<u>CT</u>	Computed tomography
<u>CVT</u>	Cortical vein thrombosis
<u>DI</u>	dopamine 1
<u>e.g.</u>	Exempli gratia
<u>EBP</u>	Epidural blood patch
<u>ECCG</u>	Electrocardiogram
<u>et al</u>	<i>et alia</i> means (and others)
<u>FDA</u>	Food and drug administration
<u>Fos</u>	Proto onco gene

<u>G</u>	Gauge
<u>gm</u>	Gram
<u>GABA</u>	Gamma amino butyric acid
<u>GON</u>	Greater occipital nerve
<u>H</u>	Hours
<u>HIV</u>	Human immunodeficiency virus
<u>HLA</u>	Human leukocyte antigen
<u>i.e</u>	id est, meaning "that is."
<u>ICP</u>	Intra cranial pressure
<u>IL</u>	Interleukin
<u>IT</u>	intra thecal
<u>IV</u>	Intravenous
<u>Kg</u>	Kilogram
<u>L</u>	Lumbar
<u>LD</u>	Lethal dose
<u>LON</u>	Lesser occipital nerve
<u>M1-4</u>	Muscarinic receptors 1-4
<u>Mg</u>	Milligram
<u>mGluR</u>	Metabotropic glutamate receptors
<u>Min</u>	Minutes
<u>ml</u>	Milliliter
<u>Mm</u>	Millimeter
<u>MRI</u>	Magnetic resonance imaging
<u>ng</u>	Nano gram
<u>NMDA</u>	N-methyl-D-aspartate
<u>NO</u>	Nitrous oxide
<u>PDPH</u>	Post dural puncture headache
<u>pmol</u>	Pico mole
<u>S</u>	Sacral

<u>5HT₁</u>	serotonin 1
<u>SD</u>	Standard deviation
<u>SIH</u>	Spontaneous intracranial hypotension
<u>T</u>	Thoracic
<u>t_{1/2}</u>	Half life
<u>TNC</u>	Trigeminal nucleus caudalis
<u>TNF-α</u>	Tumor necrosis factor alpha
<u>VAS</u>	Visual Analogue Scale
<u>VC</u>	Vertebral Column
<u>Vs.</u>	Versus

Introduction

Spinal anesthesia is a wide spread popular method of anesthesia, used for many surgical procedures, particularly in obstetric field, being easy, convenient and safe for both mother and baby ^(3,4)

However, the process of penetrating the meninges for local anesthetic introduction into the subarachnoid space may be associated with many undesirable side effects, Post dural puncture headache (PDPH) being one of the most frequent side effect occurring with the process of spinal anesthesia that varies from a mild self-limited condition to a severe distressing condition affecting the life style of the patient. ^(5,6)

Pregnant women are particularly prone to post dural puncture headache (PDPH) which is frequently severe or incapacitating and of at least several days in duration. It often interferes with maternal-infant interaction, and it is a significant cause of increased anesthetic work load and prolongs hospitalization. ⁽⁷⁾

Many studies conducted to determine the pathogenesis and possible causes of Post dural puncture headache (PDPH), but till now the pathophysiology of PDPH is still unclear. ⁽⁸⁾ The main cause is thought to be the leakage of CSF through the dural puncture, with continuous CSF leakage, decreased CSF pressure and volume occurs, however the relationship between the low CSF pressure and volume and (PDPH) is yet unclear. ⁽⁹⁾ Another theory suggests that the loss of CSF volume activates the adenosine receptors which lead to vasodilatation and headache. ⁽⁹⁾

Upon occurrence of PDPH, conservative measures such as hydration and bed rest should be started immediately but these measures have a history

Introduction

of not being very effective ⁽¹⁰⁾, therefore numerous strategies have instead been suggested to prevent Post dural puncture headache (PDPH), some are non-invasive medical treatment, such as caffeine, other are invasive either attempting to replace CSF or to seal the dural puncture site, some of these measures are: epidural saline bolus, ⁽¹¹⁾ epidural colloid patch, ^(12,13) epidural morphine injection, ⁽¹⁴⁾ epidural blood patch. ⁽¹⁵⁾

Neostigmine is a popular drug used in anesthetic practice, mainly as a part of reversal of non-depolarizing muscle relaxants, however it has a central action through the central muscarinic receptors of the spinal cord.

Administration of neostigmine via the intrathecal (IT) route causing increase in the endogenous acetyl choline with subsequent activation of these receptors .This is thought to produce analgesia and sedation beside the occurrence of some undesirable side effect such as bradycardia and nausea as well as vomiting. ⁽¹⁶⁾

Administration of neostigmine via the epidural space is readily used as an adjuvant with local anesthetics or alone to produce analgesia and sedation, with reporting of less frequent side effects. ^(17,18,19) It's also expected that its central action may interfere with the pathogenesis of post dural puncture headache (PDPH), we expect the use neostigmine could help to prevent and control its symptoms making epidural neostigmine looks a promising solution for this distressing condition.

CHAPTER I
RELATED ANATOMY

Anatomy of Vertebral Column (V.C.)

The vertebral column composed of 7 cervical, 12 thoracic, 5 lumbar, 5 fused sacral vertebrae and the coccyx, with four characteristic features: the anterior convexity in the sacral region, the lumbar lordosis, the thoracic kyphosis, and the cervical lordosis. In the lumbar area, the spinous processes project directly posteriorly while, in the thoracic area, the spinous processes project posteriorly and more inferiorly with the steepest downward angulation at the mid-thoracic level. This overlap can make the midline approach to the epidural space difficult or impossible at the T5-T9 levels. At higher thoracic levels, the spinous processes angle elevated again being nearly horizontal at C7.

The spinal canal is bounded by the vertebral bodies anteriorly, the pedicles laterally, and the ligament flava and the laminae posteriorly. The canal starts superiorly in the foramen magnum and ends inferiorly in the sacral hiatus⁽²⁰⁾.

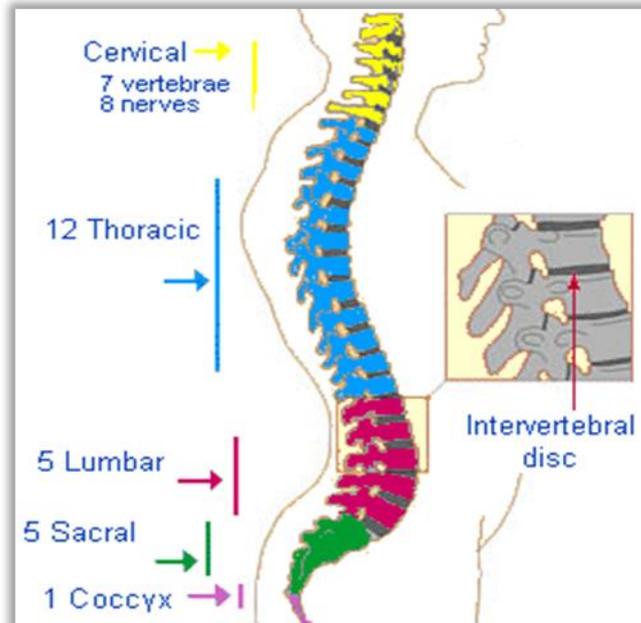


Figure 1 The vertebral column